Modern Concepts of Cardiovascular Disease

Published monthly by the AMERICAN HEART ASSOCIATION

1775 BROADWAY AT 58TH STREET, NEW YORK, N. Y.

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VOL. XVII DECEMBER, 1948 No. 12

THE RELATION OF MATERNAL INFECTION TO CONGENITAL MALFORMATIONS OF THE HEART

The problem of preventing congenital heart disease has received great impetus from the remarkable observations made by Gregg in Australia. An unusual number of children with congenital cataracts, associated in many instances with congenital heart disease, presented themselves in Sydney in the early months of 1941. Gregg discovered that one of the factors common to this group of children was the fact that their mothers had contracted German measles (rubella) during the early weeks of their pregnancies. The maternal infection coincided with an epidemic of German measles which occurred in the civilian population and army encampments alike. These initial observations were quickly confirmed by physicians in the United States and Europe, as well as Australia, so that by now many hundred cases have been reported.

The types of congenital defects that have been found in children whose mothers contracted German measles early in pregnancy include, in addition to those of the eyes and heart, deafness which is either partial or complete and may be bilateral, mental retardation that is often severe, a small body size at birth and a failure to grow and develop physically at the expected rates. A large number of other defects are less commonly seen, such as cleft palate, harelip, inguinal hernia, glaucoma and occasional genito-urinary anomalies. It is known that some babies whose mothers contract rubella in the first three months of pregnancy escape without having any evidence of a malformation, but it is not yet established how often this fortuitous result occurs.

Malformations of the heart are among the defects most frequently observed subsequent to maternal rubella. Approximately 25 to 50 per cent of the children with defects have been reported as having malformations of the heart. The discrepancy in the frequency with which cardiac defects have been reported is probably related to the fact that the diagnosis has been based in many instances simply on the presence of a systolic murmur. Since the latter is a common finding in children and it is often difficult to distinguish the functional from the organic murmur in pediatric practice, there is room for considerable disagreement in the interpretation placed upon them. Furthermore, the types of defects in the heart belong almost exclusively to the group of malformations that are not associated with cyanosis or other clinical evidence of impaired cardiac function. Consequently, opportunities for examining the hearts of these children at autopsy have not been abundant. Such postmortem examinations as have been made have revealed two general types of defects: incomplete closure of the septa or patency of the ductus arteriosus or both. One child at postmortem examination had coarctation of the aorta. The two general classes of defects found at postmortem have also been the ones repeatedly diagnosed by the clinicians. Again, it needs to be emphasized that while these two defects can frequently be diagnosed correctly by the usual type of clinical examination, there is room for error, particularly in the case of a patent interventricular septum. The clinical diagnosis of a patent ductus is far more often correctly made, because the clinical findings are more distinctive.

ANNUAL MEETING

The Annual Meeting and Twenty-second Scientific Session of the American Heart Association will be held in Atlantic City, New Jersey, on June 3 and 4, 1949. The Chalfonte-Haddon Hall will be the headquarters for all meetings and for the Annual Dinner which will take place on Saturday evening, June 4.

The Chairman of the Program Committee for the Annual Scientific Session is Doctor Eugene A. Stead, Jr., Duke University School of Medicine, Durham, North Carolina. All who desire to present papers at the meetings in Atlantic City on June 3 and 4 should forward to Doctor Stead an abstract of the proposed presentation of 250 words. The dead line for the receipt of abstracts is March 1, 1948.

The presence of septal defects or abnormalities in the aortic and pulmonary outlets in this group of children can be explained readily in the light of what is known of the embryology of the heart. During the period between the fifth and the eighth week of intra-uterine life the original common atrio-ventricular canal is divided into separate right and left channels, and the interventricular septum is formed and completely closed. Concurrently the interatrial septal complex with its compensating valvular mechanism is laid down. In the latter part of the same period the truncus arteriosus undergoes the spiral partitioning which establishes the ascending aorta and the pulmonary trunk. Theoretically the virus of German measles traverses the placental barrier and produces an injury to the heart at the time these critical morphologic changes are taking place. Hence, an attack of German measles in the second month of pregnancy is likely to involve the heart. Sometimes the heart is the only organ that has been injured, but more often the infant whose heart has been involved also will be found either to have cataracts, to be deaf, mentally retarded and small in body size or to have some combination of these several defects.

It is difficult to determine the incidence of cardiac anomalies subsequent to maternal rubella, as has been mentioned above. The diagnosis of rubella is uncertain in the absence of an epidemic and has been made in retrospect in most of the reported cases of congenital defects. The infection probably is overlooked by many who have it, because of its mildness. On the basis of available data, which admittedly are imperfect, probably about 5 per cent of congenital cardiac defects can be ascribed to maternal rubella. These are of the acyanotic type. Cases have been reported in which the child was cyanotic and a tetralogy of Fallot was thought to be present, but these have not been confirmed by postmortem studies or by any operative procedure.

The observations on the relationship of congenital malformations to maternal rubella has naturally raised the question as to whether or not other infectious diseases, especially those of viral origin, could not have an affinity for fetal tissues. The relative ease with which it is possible to grow viruses on embryonic tissue has served only to encourage thinking along these lines. The efforts to indict other viruses has not met with anything like the success as found in the case of rubella. The case reports are still too few, but so far as they have gone, it has not been possible to show that measles, mumps, chicken pox and poliomyelitis play a role similar to that of rubella. There has been some effort to relate the viruses of the common cold and other infections of the upper part of the respiratory tract to the presence of congenital malformations in the fetus, but these viruses are so ubiquitous that the opportunity for a chance relationship precludes their acceptance as a causal factor unless the virus or viruses can be specifically identified. The possibility that viruses other than rubella injure the fetus without killing it still exists. Infectious mononucleosis, which probably is a virus infection, has been reported as involving the heart in 3 of 4 infants whose mothers contracted the disease in the first ten weeks of pregnancy. This is a promising lead that deserves further study, but it can not be considered as anything more than a suggestion at the present time.

Considerable interest attaches itself to the epidemiology of German measles. There is some evidence that this mild infection occurs in annual outbreaks in the spring in many sections of the United States at the same time. There are larger epidemics which evidently occur about every decade and these also seem to appear simultaneously in the spring of the year throughout most of the United States. The above-mentioned evidence is partly based on the observation that the birthdays of children born subsequent to an attack of maternal rubella fall most frequently in the months of November and December. The pattern of births repeats itself from year to year and is based on births reported from widespread areas in this country. Aycock and Ingalls found that over a period of thirty years there were outbreaks of rubella in Massachusetts with sharp peaks of prevalence recurring in April and May of each year. This pattern fits very well with the observation on the birthdays of children reported as having been born subsequent to maternal rubella. In 1943 there evidently occurred one of the large epidemics seen about every decade. It is known that the epidemic of 1943 was prevalent in many sections of the United States that year and judging from the birthdays of involved children, this epidemic also occurred in the spring in simultaneous fashion.

The epidemiology of Germany measles has now become an important matter. More accurate information concerning it will permit a more intelligent planning of studies designed to determine the incidence of defective children who are born to mothers contracting the disease in the first trimester of pregnancy. It should help also in planning for the prevention of the disastrous consequences to the fetus. The only way known at the present time of accomplishing this desirable end is to expose as many girls as possible to the infection before they have reached the child-bearing period. While reinfection undoubtedly occurs, as in most other virus diseases of this kind, such instances are probably uncommon. As far as is known, one infection with the virus of German measles gives a high degree of immunity. The risk involved to the child who contracts German measles is practically nil; it is one of the lowest of any of the recognized exanthems. There is no question that German measles acquired in childhood would be a welcome means of ridding the population of the devastating effects visited on some of the unborn children of mothers unfortunate enough to have acquired this infection in the first three months of pregnancy.

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